



US006258339B1

(12) **United States Patent**
Schutt et al.(10) **Patent No.: US 6,258,339 B1**
(45) **Date of Patent: *Jul. 10, 2001**(54) **OSMOTICALLY STABILIZED
MICROBUBBLE PREPARATIONS**(75) **Inventors:** Ernest G. Schutt, San Diego; David P. Evitts, La Jolla; Rene Alta Kinner, San Diego, all of CA (US); Charles David Anderson, Lebanon, NJ (US); Jeffry G. Weers, San Diego, CA (US)(73) **Assignee:** Alliance Pharmaceutical Corp., San Diego, CA (US)(*) **Notice:** This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) **Appl. No.:** 08/841,847(22) **Filed:** May 5, 1997**Related U.S. Application Data**

(63) Continuation of application No. 08/405,447, filed on Mar. 16, 1995, now Pat. No. 5,639,443, which is a continuation of application No. 08/099,951, filed on Jul. 30, 1993, now abandoned.

(51) **Int. Cl.⁷** A61B 8/13(52) **U.S. Cl.** 424/9.51; 424/9.52(58) **Field of Search** 424/9.52, 9.51; 600/431, 458(56) **References Cited****U.S. PATENT DOCUMENTS**

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Primary Examiner—Michael G. Hartley(74) **Attorney, Agent, or Firm**—Knobbe, Martens, Olson & Bear, LLP(57) **ABSTRACT**

A microbubble preparation formed of a plurality of microbubbles comprising a first gas and a second gas surrounded by a membrane such as a surfactant, wherein the first gas and the second gas are present in a molar ratio of from about 1:100 to about 1000:1, and wherein the first gas has a vapor pressure of at least about (760-x) mm Hg at 37° C., where x is the vapor pressure of the second gas at 37° C., and wherein the vapor pressure of each of the first and second gases is greater than about 75 mm Hg at 37° C.; also disclosed are methods for preparing microbubble compositions, including compositions that rapidly shrink from a first average diameter to a second average diameter less than about 75% of the first average diameter and are stabilized at the second average diameter; kits for preparing microbubbles; and methods for using such microbubbles as ultrasound contrast agents.

101 Claims, No Drawings